Amendments to the Specification

Please amend the paragraph on page 9, lines 15-19 of the specification, as follows:

The other subfamily of the compounds of the present invention with the general formulae **3DX-3DXVII**, includes conjugates of conformationally restricted, cyclic and branched (dimeric) polyamines with acidic retinoids. Restriction of conformation in the polyamine moiety is imposed by e.g. aromatic rings incorporated in the chain (conjugates **3DX** and **3DXI**) or heterocyclic rings (conjugates **3DXII**) whereas the cyclic polyamines used are of various ring-sizes and contain different numbers of carbon, nitrogen and oxygen atoms in the ring (conjugates **3DXIII-3DXVI**). In this subfamily, the polyamine moiety also consists of symmetric or asymmetric polyamine (spermine and spermidine) dimers (conjugates **3DXVII**). In this category of compounds, the substituent R is one of the above mentioned ~~R.sup.1-R.sup.6~~, R^1-R^6 preferably R^1 ~~R.sup.1~~, whereas n is one of the numbers 1, 2 and 7. In compounds **3DXVIIA,** R' is identical to R" and equal to COR. In compounds **3DXVIIB,** R' is also identical to R" but equal to ~~(CH.sub.2).sub.3NHCOR~~ $(CH_2)_3NHCOR$. Finally, in compounds **3DXVIIC,** R' is equal to COR and R" is equal to $(CH_2)_3NHCOR$.

Please amend the paragraph [0028] of the current specification, U.S. Patent Application Publication No. 2006/0189696, as follows:

Key-reaction in the synthesis of the polyamine amides described in the present invention is the coupling of an acidic retinoid or activated derivatives of an acidic retinoid with either a free polyamine (direct method) or a suitably protected derivative of a polyamine (indirect method). The acidic retinoids used in this work were either commercially available, e.g. all-trans-retinoic acid (ALDRICH), 9- and **13**-cis-retinoic acid (SIGMA) and acitretin (ROCHE) or synthesized using standard reactions, e.g. the polyene chain-shortened all-trans-retinoic acid analogues **9** and **10** depicted in **FIG. 2**. In particular, ß-ionylideneacetic acid **(9)** was obtained according to a published protocol (Tietze und Eicher, `Realctionen und Synthesen im organisch-chemischen Praktikum`, Thieme, New York, 1981, p 445), whereas ß -ionylidene-trans-crotonic acid **(10)** was synthesized from ß -ionylidenethanol (previous reference, p. 446) through a three-

steps protocol involving oxidation to the corresponding aldehyde with o-iodoxybenzoic acid (IBX) in DMSO (Frigerio et al, J. ORG. CHEM., 60, 7272 (1995)), Wittig reaction with diethyl (ethoxycarbonyl)methylphosphonate and finally saponification. ~~Taleing~~ Taking into consideration the sensitivity of retinoids towards strongly acidic reagents, we chose to activate the acidic retinoids in the form of their corresponding 'active' esters with N-hydroxysuccinimide (HOSu) which are hydrolytically relatively stable and can be readily purified, if necessary, with flash column chromatography (FCC). In addition, the succinimidyl esters of α, β-unsaturated carboxylic acids react only with the primary amino group of polyamines (Papaioannou et al, TETRAHEDRON LETT., 43, 2593 (2002)). The succinimidyl esters of acidic retinoids (**21**) are simply obtained (**FIG. 3**) by treating the acidic retinoid with HOSu in the presence of the coupling agent N,N'-dicyclohexylcarbodiimide (DCC) (see EXAMPLE 1). The succinimidyl esters **21** thus obtained are of sufficient purity to be used in the next step. However, pure samples can be readily obtained through purification with FCC. Esters **21** are then used to acylate the primary amino groups of either the free polyamines (direct method) or polyamines protected at their secondary amino functions with protecting groups, such as 9-fluorenylmethoxycarbonyl (Fmoc) or trifluoroacetyl (Tfa), which can be subsequently removed under basic conditions (indirect method). Examples of both methodologies in the preparation of linear N^{α}-mono(3DII)- and N^{α}, N^{ω} -diacetylated tetra-amines (3DI and 3DVIII) and N^{α}, N^{ω} - diacetylated triamines (3DIV) and hexa-amines (3DIX) are presented in **FIG. 4** and detailed under the EXAMPLES 2 and 3. Useful precursors for the indirect methodology are polyamines bearing the triphenylmethyl (trityl, Trt) protecting group at their terminal amino functions, like **22, 26** and **27**, whose preparation has been described by one of the inventors using the amide approach for the assembly of the polyamine chain (Papaioannou et al, TETRAHEDRON LETT., 36, 5187 (1995); 39, 5117 (1998); 42, 1579 (2001); 43, 2593 and 2597 (2002) and Papaioannou et al, in `Drug Discovery and Design: Medical Aspects`, J. Matsoulkas and T. Mavromoustakos (Eds.), IOS Press, Amsterdam, 2002, in press). These precursors are then routinely protected at their secondary amino function(s) with e.g. the Fmoc group and finally detritylated by a solution of trifluoroacetic acid (TFA) in dichloromethane (DCM). Mono- and/or bisacylation is then performed using one or two equivalents of esters **21**, respectively. Finally, secondary amino group deprotection is carried out using a 20% solution of piperidine (Pip) in DCM, following routine purification of the fully protected intermediates by FCC, if necessary.

Please amend paragraph [0036] of the current specification, U.S. Patent Application Publication No. 2006/0189696, as follows:

[0036] The examples below are given so as to illustrate the practice of this invention. They are not intended to limit or ~~define~~ define the entire scope of the invention.